

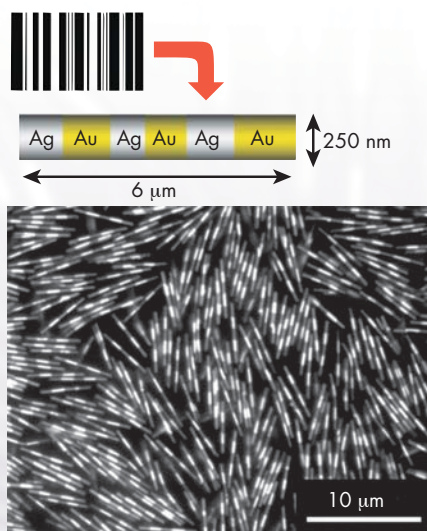
# Microfluidic System for Solution-Array-Based Bioassays



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**W**e are developing an integrated, reconfigurable microfluidic system for performing user-specified multiplexed biomarker assays for the early detection of disease using solution array technology. Solution arrays are similar to gene and protein chips, but use surface functionalized particles in solution, rather than the binding of biomolecules to a fixed surface. Instead of correlating fluorescence with location, as in a chip format, the particles are encoded for identification. Results are read by examining particles for their encoded type and for the presence or absence of the fluorescence indicative of a positive binding event. The flexibility of solution arrays means that different types of functionalized particles can be added as desired by an end user, and particles for DNA, RNA, and protein detection can be used simultaneously in a single low-cost format.

**Figure 1.** Optical microscope image of Nanobarcodes™ particles. The light and dark stripes are due to alternating bands of gold and silver metal, having different reflectivities at the observation wavelength.



The particles used in this project are Nanobarcodes™ particles (Fig. 1), short metallic nanowires that bear patterns of light and dark stripes analogous to the stripes in a supermarket barcode. These particles offer unique advantages in their ability to be identified using standard light microscopy, avoiding the need for complicated spectroscopic or flow cytometry methods. Surface functionalization of metal particles is understood, and the Nanobarcodes™ can be made with magnetic materials, opening up new possibilities for manipulating, transporting, and trapping the particles using magnetic and electric fields.

## Project Goals

The goal of the project is to demonstrate a prototype bioassay system based on Nanobarcodes™ particles. This system will be capable of performing simultaneous assays for several biowarfare agent simulants. Along the way, we expect to achieve a number of important scientific goals, advancing the state of the art in particle-based biochemical assays and in the manipulation and control of metallic nanoparticles within aqueous solutions.

## Relevance to LLNL Mission

Biodefense is a major research thrust at LLNL, in support of technology needs for homeland security and national defense. The technology developed in this project will also benefit medical diagnosis and treatment of disease.

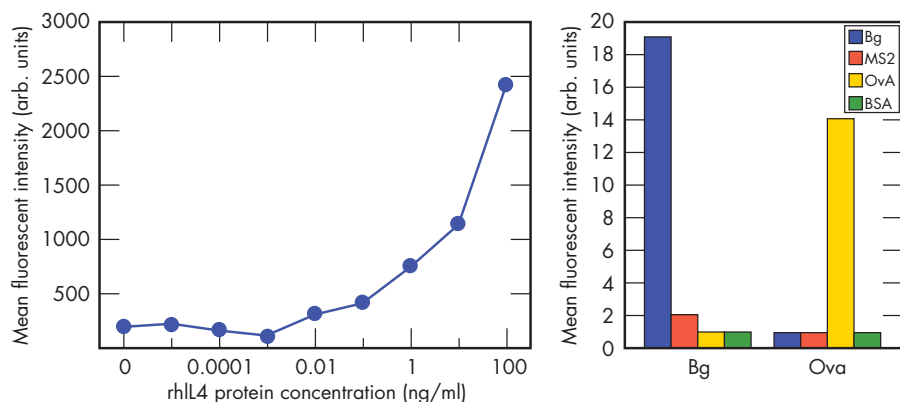
### FY2004 Accomplishments and Results

The project has made several important advancements in the past year. First, multiplex immunoassays have been successfully implemented in the Nanobarcode™ format. The first implementation, using medical-grade cytokine antigens and anti-cytokine antibodies, demonstrated that the sensitivity of the Nanobarcode™-based assay is similar to that of the best state-of-the-art immunoassays (Fig 2.). The second

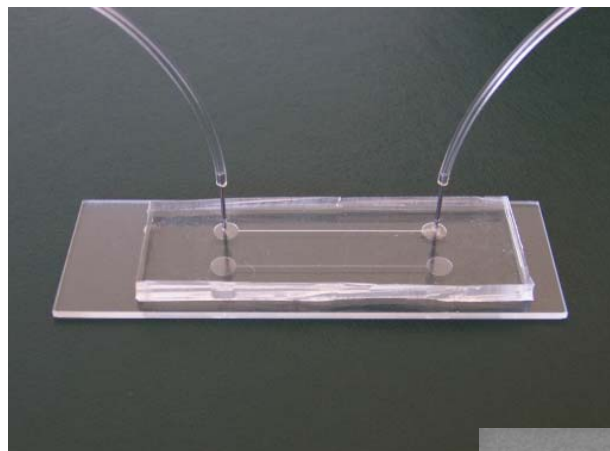
implementation used a panel of bio warfare agent simulants and demonstrated that the approach works with these types of reagents as well.

Progress was also made in the area of fluid transport and electromagnetic manipulation of the particles. Tests of functionalized particle transport through glass and silicone channels (Fig. 3) show minimal particle adhesion, and both experimental studies and computer modeling work have

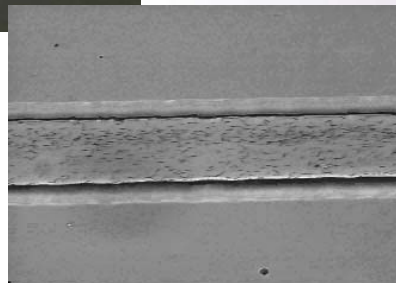
advanced our abilities to move and align particles using AC and DC electric fields as well as magnetic fields. In addition, experiments have revealed new, important data about the electrokinetic properties of functionalized metallic nanoparticles in aqueous suspension. Finally, we have demonstrated an effective means of using self-assembly to organize the Nanobarcode™ particles into a 2-D array for improved optical readout.



**Figure 2.** Nanobarcode™-based bioassay results. (a) Plot of fluorescence signal vs. antigen concentration for a cytokine target, showing sensitivity in the 10 pg/ml range. (b) Plot of a four-plex biodetection panel showing the specificity of response to *Bacillus globigii*, a bacterial spore, and Ovalbumin, a soluble serum protein.



**Figure 3.** A typical glass/PDMS microfluidic test structure, and an associated micrograph showing Nanobarcode™ flowing adhesion-free through the 50-µm channel.



### Related References

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2. Keating, K. D., and M. J. Natan, "Striped Metal Nanowires as Building Blocks and Optical Tags," *Adv. Mater.*, **15**, pp. 451-454, 2003.
3. Dougherty, G. M., F. Chuang, K. Rose, S. Pannu, S. Penn, and M. Natan, "Multiplex Biodetection Using Solution Arrays Based on Encoded Nanowire Particles," *Materials Research Society Spring Meeting*, San Francisco, California April 12-16, 2004.

### FY2005 Proposed Work

The final year of the project is devoted to integrating what we have learned into a working demonstration system that can carry out full biodetection tests using the Nanobarcode™-particle-based solution assay. Work in the bioassay area will focus on optimizing the process performance within the microfluidic system. Electromagnetic manipulation and 2-D array formation will be included within the bioassay process flow. The complete system will be capable of performing biodetection assays, as well as extracting and reading Nanobarcode™ particles from liquid suspensions for applications in forensics and other homeland security applications.